PLMA
PRIVATE LABEL MANUFACTURERS ASSOCIATION

November 4, 1999

BY TELECOPY: (301) 827-6870

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, Maryland 20852

Re: 180-Day Generic Drug Exclusivity For Abbreviated New Drug Applications
Docket No. 85N-0214

Ladies and Gentlemen:

On behalf of the Private Label Manufacturers Association ("PLMA"), I am writing to comment on the proposed rules ("proposed amendments") regarding the 180-Day Generic Drug Exclusivity for Abbreviated New Drug Applications ("180-Day Exclusivity Rule"), 64 Fed. Reg. 42873 (August 6, 1999). PLMA requests that you consider our comments and include them in the formal record of the proceeding.

PLMA is a major trade association representing over 3,200 companies which are involved in the manufacture and distribution of private label or store brand products, i.e., items sold under the retailer's or wholesaler's brand name in drug chains, supermarkets and mass merchandisers throughout the United States. Store brand products include: over-the-counter drugs, health and beauty care

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items, packaged and processed foods, beverages, snacks, household cleaners, outdoor and leisure products, auto aftercare and a wide range of other general merchandise. Many of PLMA's members are also involved in the manufacture of private label or generic pharmaceutical products, including both prescription and over-the-counter products.

For the fifty-two (52) week period ending December 31, 1998, store brands accounted for $2.9 billion in drug chain sales and 13.4% of drug chain unit sales. At supermarkets, store brands accounted for $35.4 billion in sales and 19.9% of unit sales. With respect to mass merchandisers, store brands accounted for $5.0 billion in sales and 11.8% of unit sales (PLMA's 1999 Private Label Yearbook; statistics compiled by Information Resources, Inc.). Overall, private label accounts for over $43 billion in annual sales at U.S. drug chains, supermarkets, and mass merchandisers combined -- approximately one out of every five products sold is a store brand.

From the consumer's point of view, store brands and generics represent substantial savings for products of comparable or superior quality and performance to the leading national brands. Typical of the savings that consumers enjoyed in 1997 were $423

million for vitamins and $339 million for disposable diapers. Purchasers of store brands saved some $15.8 billion in drug chains, supermarkets, and mass merchandisers in 1997 (PLMA's 1998 Private Label Yearbook).

PLMA supports the Food and Drug Administration's ("FDA") attempts to clarify the 180-day generic drug exclusivity provisions of the Federal Food, Drug and Cosmetic Act ("Act") and the existing eligibility requirements for abbreviated new drug applications ("ANDA"). PLMA also supports many of the FDA's proposed amendments believing that, for the most part, the proposed amendments clarify the existing rules and more fully align the existing rules with Congress' intent in enacting the Act.

PLMA, however, is concerned that several of the proposed amendments as drafted will not permit the prompt entry of generic drug products into the market and will impair competition in the generic drug industry. PLMA therefore submits the following observations and recommendations with respect to the proposed amendments:

I. Only The First Applicant Is Eligible

PLMA is unable to support the proposed amendment which clearly states that only the first applicant to file an ANDA with a paragraph IV certification is entitled to the 180-day period of exclusivity, regardless of circumstances and regardless of whether the first applicant's ANDA is determined to be "substantially complete" (see infra Section II).

This proposed amendment permits the filing of an incomplete application in order to block subsequent filers of ANDAs with paragraph IV certification from obtaining exclusivity. For example, under the proposed amendments, if the first filed applicant must conduct a new bioequivalence study to obtain approval of the ANDA, the application will not be considered to be "substantially complete" and the first filed applicant will not be eligible for exclusivity. Thereafter, no other applicant with a paragraph IV certification will be eligible for exclusivity for that drug product. Similarly, it is conceivable that a manufacturer will deliberately file an incomplete application in order to prevent another generic manufacturer from obtaining a 180-day exclusivity period. This may result in abuse of the system and thwart Congress' intention to create an incentive for proper patent challenges to open up the generic drug market. The proposed

amendment should be revised to discourage the filing of incomplete applications. A subsequent applicant which files a "substantially complete" ANDA with a paragraph IV certification should not be precluded from receiving 180-day exclusivity simply because the first filed applicant filed, deliberately or otherwise, an inadequate application.

PLMA recognizes that by permitting a subsequent filer of an ANDA with paragraph IV certification to be entitled to exclusivity, the proposed amendment may further delay entry into the market for generic drug products. As a result, PLMA suggests that "rolling exclusivity" or the granting of exclusivity to a later applicant that files a substantially complete ANDA with a paragraph IV certification should be permitted to receive exclusivity only upon the first filed application being found by the FDA not to be "substantially complete."

PLMA would like to propose an alternative to the "first to file" entitlement to exclusivity. While not discussed in the proposed amendments, PLMA requests that the FDA consider a rule which would award exclusivity based on the first approved ANDA with paragraph IV certification. Not only would this encourage applicants to file ANDAs with paragraph IV certifications, but it

would also encourage applicants to expedite the FDA's approval process by providing all required information in a timely fashion. By adopting a rule based on application approval, later filed applicants will not be prejudiced by first filed applications which are not "substantially complete" or are otherwise defective.

II. The ANDA Must Be "Substantially Complete"

PLMA supports the position that the ANDA must be substantially complete in order to entitle the manufacturer to exclusivity. However, PLMA is concerned that the term "substantially complete" is not adequately defined in the proposed amendments. The FDA should ensure that this term is given a clear and concise definition so as to eliminate confusion and argument concerning whether an application is, in fact, "substantially complete."

Moreover, a determination by the FDA as to whether an ANDA is substantially complete should be made at the time of the application's filing. This will prevent arbitrary amendments to an otherwise incomplete application in order to make the application "substantially complete" after its filing.

III. Multiple Patents For The Same Drug

PLMA supports the proposed amendment which states that if there are multiple patents for a listed drug, the applicant submitting the first ANDA with a paragraph IV certification to any of the listed patents will be the only applicant eligible for exclusivity for that drug. PLMA's support for this proposed amendment stems from the fact that this proposed amendment will promote early entry into the generic drug market. As noted by the FDA, the granting of multiple exclusivities could further foreclose the market, preventing the entry of generic drugs into the market. This result should not be permitted and the proposed amendment correctly permits exclusivity only to the applicant submitting the first paragraph IV certification.

IV. First Applicant Not Eligible For Exclusivity If Sued And Loses Lawsuit

PLMA supports an express prohibition against awarding exclusivity to the first applicant that files a substantially complete ANDA with a paragraph IV certification if that applicant is sued by the patent holder and loses the litigation. PLMA also supports the FDA's interpretation of the statute that if the first applicant is ineligible for exclusivity because it was sued by the patent holder and lost, then no applicant would be eligible for

exclusivity. This interpretation encourages early entry of generic drugs and increases competition in the generic drug industry.[1]

V. Shared Exclusivity For Multiple ANDA Applications Filed On The Same Day

PLMA is unable to support the proposed amendment that all applicants filing ANDAs containing paragraph IV certifications for a particular drug product that are received on the same day will be eligible for exclusivity if no other ANDA with a paragraph IV certification for the drug product has been previously filed. PLMA believes that a better rule is that if a true exclusivity cannot be awarded to an identified first filer then no exclusivity should be awarded to any applicant when more than one ANDA is received on the same day. This rule is consistent with Congress' intent and increases competition in the generic drug industry.

PLMA also believes that a one day time period for determining whether multiple applications were filed "simultaneously" is too short and that the FDA should designate a longer time period, i.e., ten (10) or twenty (20) days from the date of the

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[1] Contrary to the situation discussed supra in Section I, this scenario is not open to abuses by applicants seeking only to prevent others from obtaining exclusivity. Accordingly, there is no need for an exception allowing for rolling exclusivity in this instance.

first filing, to determine whether there has been a filing of multiple applications.

It is our understanding that the purpose of the 180-day exclusivity period is to encourage generic manufacturers to step forward, out of the crowd, and challenge existing patents. The fact that one manufacturer steps forward only a day or two before another manufacturer should not entitle the first manufacturer to exclusivity to the complete exclusion of the second manufacturer. Therefore, if several manufacturers step forward simultaneously, no one manufacturer should be entitled to exclusivity. Moreover, as discussed above, multiple exclusivities are inefficient and may seriously hinder competition. Accordingly, to the extent that multiple applications are filed, no applicant should be entitled to exclusivity.

VI. Length Of Triggering Period

PLMA supports the FDA's suggestion of an alternative, shorter triggering period of sixty (60) days. The purpose of the triggering period is to prevent delay and promote early entry into the generic drug market. Therefore, PLMA supports the shortest effective triggering period in all situations.

PLMA welcomes a future opportunity to comment on specific language establishing an abbreviated triggering period.

VII. Prompt Approval And Marketing

PLMA disagrees with the FDA's proposed deletion of the requirement that the first filed applicant must actively pursue approval of its ANDA, or the agency may immediately approve any subsequent ANDA eligible for final approval. The present requirement is necessary to prevent abuse by a first applicant which submits its application solely in order to prevent another applicant from obtaining exclusivity and which has no intention of pursuing FDA approval of its application.

VIII. Waiver Of Exclusivity

PLMA supports the FDA's position that the first filed applicant should be entitled to waive its right to exclusivity. However, as written, the proposed amendment only permits waiver during the exclusivity period. PLMA does not see a reason to distinguish between the exclusivity period and the trigger period. The first applicant should be entitled to waive exclusivity at any time after receipt of such exclusivity.

In sum, while PLMA supports the FDA's intent to clarify the current regulations, it is the opinion of PLMA that the current language of several of the proposed amendments will not accomplish the FDA's goals. In fact, PLMA fears that the Act, coupled with the proposed amendments, will inadvertently result in a less competitive industry wrought with manipulation and delay. Accordingly, PLMA requests that the FDA revise the proposed amendments to address the issues outlined herein.

Thank you for considering our concerns with respect to the proposed amendments.

Respectfully yours,

Brian Sharoff

Brian Sharoff
President

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RE: Docket No. 85N-0214

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November 4, 1999

Dockets Management Branch (HFA - 305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: Docket No. 85N-0214; Proposed Rule entitled "180-Day Generic Drug Exclusivity for Abbreviated New Drug Applications," 64 Fed. Reg. 42,873 (August 6, 1999)

Dear Sir or Madam:

These comments on the above-referenced rule are being submitted on behalf of clients who hold approved Abbreviated New Drug Applications (ANDAs) and who are entitled to 180 days of exclusivity under section 505(j)(5)(B)(iv) of the Federal Food, Drug, and Cosmetic Act (FDC Act). These comments are limited strictly to the Food and Drug Administration's (FDA's) Proposed Implementation Plan (PIP) for the proposed rule. In submitting these limited comments on only one aspect of the proposed rule, we are not conceding that FDA has the statutory authority to revise its existing regulations as proposed.

The PIP reads as follows:

> The agency proposes that any final rule based on this proposal take effect 30 days after its publication in the Federal Register. The agency proposes to apply the provisions of any final rule to ANDA's

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> pending as of the effective date and to ANDA's that are submitted after that date.

64 Fed. Reg. at 42882.

Assuming that a "pending" ANDA is one that has been submitted to FDA but has not yet been approved, the PIP fails to address an issue of critical importance. How will the revised regulation apply to ANDAs that are pending or submitted after the effective date of the final rule when another approved ANDA has already qualified for 180 days of exclusivity prior to the effective date of the final rule? It is our position that any final rule should not affect the exclusivity of an ANDA that was approved prior to the effective date of the rule. FDA should make clear in the final rule that the rule will not affect the 180-day exclusivity of an ANDA approved prior to the effective date of the rule. Any other decision by FDA would violate the general principle that regulations are not to be given retroactive effect and would result in an unconstitutional taking of property in violation of the Fifth Amendment to the Constitution.

The following discussion illustrates our concern in greater detail. Assume that Company A is the first applicant to submit an ANDA with a paragraph IV certification for a reference listed drug. Assume further that Company A's ANDA is approved prior to the effective date of any final rule published as a result of this proposal. Under the statute as well as FDA's implementing regulations, Company A is entitled to exclusivity that runs for a period of 180 days and can be triggered by the earlier of two events. The first possible trigger is Company A's first commercial marketing of the drug.[1] Exclusivity would run for 180 days from that date. The second trigger is the final decision of a court holding that the patent that was the subject of Company A's paragraph IV certification is invalid, unenforceable, or not infringed.[2] As before, exclusivity would run for 180 days from that date.

The proposed rule would add "triggering periods" for ANDAs pending as of or submitted after the effective date. Although the proposed rule purports to apply only to ANDAs submitted after, or pending on, the effective date of the final rule, it is not clear if FDA envisions that the proposed triggering periods are intended to apply to ANDAs that were approved prior to the effective date. For example, if Company A's first-filed ANDA were approved and entitled to exclusivity prior to the effective date, and Company B's

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1 21 U.S.C. § 355(j)(5)(B)(iv)(I); 21 C.F.R. § 314.107(c)(1)(i).

2 21 U.S.C. § 355(j)(5)(B)(iv)(II); 21 C.F.R. § 314.107(c)(1)(ii).

subsequent ANDA gained tentative approval after the effective date of the final rule, and no other obstacle lay in its path to the market other than the first ANDAs exclusivity, would the proposed triggering period of 180 days be applicable?[3] If so, Company A would have 180 days to market its product. If it did so, it would enjoy 180 days of exclusivity from the first day of commercial marketing.[4] If Company A did not proceed to market within the 180-day triggering period, it would lose its exclusivity.[5] Such a result would irreparably injure ANDA applicants that are contractually bound not to market their generic products as a consequence of a settlement of a patent infringement lawsuit.

Under the statute, an ANDA applicant who is sued for patent infringement can settle that lawsuit with the innovator by agreeing not to market its generic product for a specified period of time. While FDA may not like this result, these companies – both generic and innovator – have entered into these settlement agreements with a clear understanding of the rules that apply to 180-day exclusivity. We are concerned that 180-day exclusivity, granted before the final rule is effective – in fact, before the proposed rule was published – can be triggered under the proposed rule's terms if a subsequent ANDA, filed or pending after the effective date, receives tentative approval. We ask that the agency clarify its position on first-filed ANDAs approved prior to the effective date of the rule, and that FDA preserve the exclusivity in accordance with the two statutory triggers in section 505(j)(5)(B)(iv) of the FDC Act. If left unaddressed, this ambiguity as to the treatment of exclusivity granted before the proposed rule and its implementation may result in a regulation that operates retroactively without properly delegated authority, as well as in an unconstitutional regulatory taking.

I. Congress did not delegate to the Secretary the authority to enact retroactive regulations with regard to ANDAs

It is a general principle of statutory and regulatory interpretation that a law is not retroactive without express congressional intent[6] and a regulation is not to be applied retroactively unless Congress gave an agency explicit authority to do so.[7] The FDC Act

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3 64 Fed. Reg. at 42886 (proposed § 314.107(c)(5)(i)(A)).

4 Id.

5 64 Fed. Reg. at 42886 (proposed § 314.107(c)(5)(ii)).

6 See Landgraf v. USI Film Products, 511 U.S. 244 (1994).

7 See Bowen v. Georgetown University Hospital, 488 U.S. 209 (1988).

does not contain any grant of retroactive rulemaking authority. Nowhere in Congress' delegation of authority is there any mention of retroactivity. Unless expressed otherwise by Congress, its delegation of agency authority to promulgate regulations is strictly prospective.[8]

Georgetown merits discussion because of its clear application to this situation. In that case, the Secretary promulgated retroactive Medicare regulations to set cost limits for government reimbursement of health care service providers based on 42 U.S.C. § 1395x(v)(1)(A), which reads as follows:

> Such regulations shall . . . (ii) provide for the making of suitable retroactive corrective adjustments where, for a provider of services for any fiscal period, the aggregate reimbursement produced by the methods of determining costs proves to be either inadequate or excessive. (emphasis added).

Despite the use of the word "retroactive" in the statute, the court found that the law did not confer the authority upon the Secretary to promulgate retroactive regulations. It held, instead, that "a statutory grant of legislative rulemaking authority will not, as a general matter, be understood to encompass the power to promulgate retroactive rules unless that power is conveyed by Congress in express terms."[9]

Although the express terms of the statute seemed to indicate retroactive authority, the court held that the statute "directs the Secretary to establish a procedure for making case-by-case adjustments to reimbursement payments," rather than promulgating retroactive regulations that applied to all health care service providers.[10] The court referred to the wording of the statute, specifically the phrase "for a provider" and the word "adjustment."[11] The phrase "for a provider" indicated that each provider was to be considered individually for its reimbursement adjustment.[12] Use of the word "adjustment"

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8 Id.

9 Georgetown, 488 U.S. at 208.

10 Georgetown, 488 U.S. at 209

11 42 U.S.C. § 1395x(v)(1)(A)(ii).

12 Georgetown, 488 U.S. at 210.

rather than the word "regulation" further proved to the court that Congress had not contemplated delegation of retroactive rulemaking authority in this statute.[13] The court held that the sentence in which the word "retroactive" appeared indicated a delegation of retroactive adjustment authority only in the case of individual providers, rather than in the context of a rulemaking that would apply to all providers.[14]

Applying Georgetown to the present situation, it is impossible to find retroactive regulatory authority under the statutory provisions cited by FDA as the authority to promulgate this regulation.[15] Therefore, there is no question of statutory construction, being that Congress included absolutely no retroactive language in any part of the statutory provisions cited by FDA.

Justice Scalia's concurring opinion in Georgetown offers a more compelling view on retroactive rulemaking authority. He holds that the Administrative Procedure Act[16], (APA), in its definition of "rule," does not allow retroactive effect, no matter how reasonable the retroactive effect might be.[17] A rule is strictly prospective in nature, given the inclusion in its definition of the words "future effect."[18] Allowing retroactive rulemaking would "make a mockery . . . of the APA."[19]

The PIP, as written, does not address the proposed rule's effect on first-filed ANDAs that were approved prior to the rule's effective date. FDA states only that the final rule will apply to ANDAs pending as of or submitted after the effective date. FDA does not state clearly whether it intends to apply the rule in a way that would permit ANDAs

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13 Id.

14 See Id.

15 FDA cited as authority for these regulations: 21 U.S.C. §§ 321, 331, 351, 352, 353, 355, 371, 374, 379e. Only § 371 expressly grants FDA rulemaking power and that provision says nothing about retroactivity.

16 5 U.S.C. §§ 551 *et seq.*

17 See Georgetown, 488 U.S. at 220, Scalia, J. concurring.

18 Id.

19 Id. at 225, quoting the holding of the lower court in this case, the District of Columbia Circuit Court, 261 U.S. App. D.C. 262, 270.

that are filed after or pending on the effective date of the final rule to be used to begin a triggering period for an ANDA that was approved before the effective date. If it is FDA's intention to apply the triggering period provision in this manner, that construction would not be within the agency's delegated authority, because the rule would operate retroactively beyond the scope of Congress's delegation. FDA should therefore clarify the PIP to make clear that the final rule will not be construed to affect ANDAs whose exclusivity was granted under the current regulatory scheme.

II. A retroactive implementation of this rule could amount to an unconstitutional taking

Generic and innovator drug manufacturers have been involved in numerous lawsuits resulting from paragraph IV certifications. Many of these lawsuits have been settled based on the innovators' and generics' knowledge of the requirements for 180-day exclusivity set out in the statute and current FDA regulations and policies. The retroactive application of the proposed rule on 180-day exclusivity would impose a significant burden on innovators and generics that have entered into settlement agreements based on their rights to exclusivity and the timing thereof. A change in those rights could allow subsequent ANDAs to enter the market, depriving many first-filed ANDA holders of their exclusivity. Losing that exclusivity would result in significant uncompensated monetary losses to the first-filed ANDA holders. The Fifth Amendment to the Constitution forbids the taking of private property for public use without just compensation. Those losses would thus amount to an unconstitutional taking under the Fifth Amendment.

Case law shows that regulatory takings are judged upon "the character of the governmental action, its economic impact, and its interference with reasonable investment-backed expectations."[20] The last factor, "reasonable investment-backed expectations," formed the crux of the holding in Ruckelshaus. The court held that the plaintiff could not have reasonably expected the loss of private intellectual property resulting from a change in regulations.[21] In the same manner, generics and innovators have "reasonable investment-backed expectations" that their patent litigation settlements would not be abrogated by a retroactive change in FDA's regulations.[22] ANDA applicants could not

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20 Ruckelshaus v. Monsanto, 467 U.S. 986, 1005 (1984), quoting PruneYard Shopping Center v. Robins, 447 U.S., at 83.

21 Ruckelshaus, 467 U.S. 986, 1010-11.

22 FDA notes, in the proposed rule's preamble, that it has been regulating "directly from the statute when making exclusivity decisions on a case-by-case basis." 64

have forecast the proposed rule on 180-day exclusivity and its significant changes to market exclusivity when they settled conflicts with innovator companies. They could not have known about the prospect that subsequent ANDAs might trigger their exclusivity while they are bound by settlement agreements with innovators not to go to the market.

The Supreme Court refined its opinion in Ruckelshaus in two later cases. In Nollan v. California Coastal Commission, the court requires an "essential nexus" between the condition imposed by the government and the legitimate government interest advanced.[23] In Dolan v. City of Tigard, the court requires a "rough proportionality" between the government's legitimate purpose and the method in which it goes about achieving that purpose.[24]

Following this framework of analysis, an "essential nexus" arguably exists between FDA's legitimate government interest in regulating ANDA exclusivity and the rule it has proposed. But, if it operates retroactively, that rule would impose a disproportionate burden on ANDA holders who have not gone to the market under the current regulatory scheme. That burden would result in significant losses to private corporations, losses for which the Fifth Amendment requires just compensation from the government. In order to avoid that liability, FDA should implement the new rule with regard to 180-day exclusivity prospectively, allowing current ANDA holders to proceed to market under the regulatory status that was in place at the time their ANDAs were approved.

III. Conclusion

On its face, the implementation of the proposed rule seems clear – it applies only to those ANDAs that are pending as of, or submitted after, the effective date. But FDA must address the effect that a subsequent ANDA, pending or filed after the rule takes effect, has

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Fed. Reg. 42873, 42874. Regulating from the statute in this manner, FDA should only have used the two triggers for exclusivity that Congress provided – the first commercial marketing of the drug or the final decision of a court that the patent is invalid, unenforceable, or uninfringed. 21 U.S.C. § 355(j)(5)(B)(iv). ANDA holders have relied upon those statutory triggers as the only possible triggers for their exclusivity to run. They could not have forecast so great a deviation from the statute and change in their rights as that contained in the proposed rule.

[23] 483 U.S. 825, 837 (1987).

[24] 512 U.S. 374, 391 (1994).

on a prior ANDA applicant that is entitled to 180-day exclusivity. FDA regulations should protect the first-filed ANDAs that have been granted exclusivity under the current regulatory scheme against having that exclusivity triggered by subsequent ANDAs. The PIP should be amended to achieve this goal:

> The agency proposes that any final rule based on this proposal take effect 30 days after its publication in the Federal Register. The agency proposes to apply the provisions of any final rule to ANDAs pending as of or submitted after the effective date. The provisions of the final rule will not affect the 180-day exclusivity period of any ANDAs approved prior to the effective date.

FDA should clarify this exception to the proposed rule, or else its regulation may operate retroactively, outside of the scope of the agency's authority. The effect of this retroactive operation may result in unconstitutional takings from ANDA holders who have not yet proceeded to market.

Sincerely,

Paul M. Hyman

Paul M. Hyman

PMH/PAV/dad